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Comparison of Serum Levels of AMH and FSH Before and After Unilateral and Bilateral Laparoscopic Ovarian Drilling in PCOS Women Referred to YAS Infertility Clinic

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ABSTRACT

Background & Objective: Laparoscopic ovarian drilling (LOD) is a method for ovulation induction in polycystic ovary syndrome (PCOS) patients. The aim of this study was to evaluate the serum levels of anti-Mullerian hormone (AMH) and follicle-stimulating hormone (FSH) before and after LOD in one or two ovaries in women with PCOS.

Materials & Methods: This study was a prospective cohort study. The study population included infertile women with PCOS resistant to clomiphene referred to the Infertility Clinic of Yas Hospital. They were candidates for LOD in 2016–2017. The serum levels of AMH and FSH were measured before and after three months in two groups of unilateral and bilateral LOD. Data were analyzed using Stata software.

Results: A total of 35 female patients were enrolled in the study, 18 (51.4%) in bilateral and 17 (46%) in unilateral LOD groups; the average age of patients was 27 ± 3.4 years old. AMH levels significantly (P<0.001) decreased in both unilateral and bilateral groups after LOD. FSH levels significantly (P<0.001) increased in both groups after LOD, but this increase was higher in the unilateral group than in the bilateral group, and this difference was statistically significant (P<0.001).

Conclusion: It seems women with clomiphene-resistant PCOS when underwent unilateral or bilateral ovarian drilling experienced a significant decrease in AMH and a significant increase in FSH, indicating a decrease in their ovarian reserve.

Keywords: Drilling, Polycystic ovary syndrome, Laparoscopy, Infertility

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women characterized by abnormal menstrual cycles and hyperandrogenism (1). PCOS is still the most common cause of infertility due to anovulation in patients, and clomiphene citrate is the first line of medical treatment in infertility of PCOS (2).

The rates of ovulation and pregnancy were improved to 85–70% and 35–35%, respectively, when clomiphene citrate was used (3); however, about 15–20% of women do not respond to this treatment (4).

Laparoscopic ovarian drilling (LOD) is a surgical treatment that can stimulate ovulation in PCOS patients who are resistant to clomiphene citrate (5). This method could have appropriate results in ovulation and pregnancy (83–89% and 80–70%, respectively) (6). However, studies have shown that, on average, 20–30% of women with PCOS cannot respond well to LOD, which is probably due to inadequate ovarian stromal destruction or inherent resistance of ovaries (7).

An increase in the number of punctures is associated with improved response, but the probability of risk of adhesion and premature ovarian failure (POF) is likely to increase, which has not yet been proven (8).

Several prognostic factors were evaluated to predict successful outcomes of LOD (9, 10). However, the potential risk of it leads to excessive destruction of the ovarian follicular pool, diminished ovarian reserve, or production of anti-ovarian antibodies (especially if the ovarian blood supply is accidentally damaged, or if a large number of punctures have been created) (11, 12).

Diminished ovarian reserve can be detected through hormonal blood panels, particularly in the serum levels of follicle-stimulating hormone (FSH) and anti-Mullerian hormone (AMH) (13, 14). Studies have shown that AMH and FSH independently reflect ovarian reserve (15, 16), and it is worth mentioning that AMH is a more sensitive biomarker than FSH and luteinizing hormone (LH) to monitor ovarian reserve (17, 18).

Studies which evaluate ovarian reserve markers following LOD doing have controversial results **(19, 20)**.

Therefore, considering the above-mentioned issues and the need to evaluate ovarian reserve markers after LOD in Iranian women, the aim of this study was to evaluate the serum levels of AMH and FSH before and after unilateral and bilateral LOD in infertile women with PCOS.

Materials and Methods

This study was a prospective cohort study. The study population included infertile women with clomiphene citrate-resistant PCOS referred to the Infertility Clinic of Yas Hospital in Tehran. They were candidates for LOD according to the infertility clinic protocol in 2016–2017.

Inclusion criteria included women aged 20–35 years with PCOS (according to the Rotterdam criteria), history of infertility for at least 1 year, failure of previous treatment with clomiphene citrate (150 mg/day for 5 days), absence of male infertility, absence of contraindication for laparoscopy, normal oral glucose tolerance test (OGTT), free androgen index more than 4, and LH level more than 10 or LH/FSH ratio more than 2.

Exclusion criteria included confirmation of other diseases with a similar manifestation of PCOS, women with fallopian tubes obstruction, contraindications for surgery and anesthesia, women with one ovary, history of previous ovarian surgery.

The estimated sample size was 40 with related parameters (i.e., an alpha error of 5%, study power of 90%, Pre Mean=7.4, Post Mean=4.2, SD Pre Mean=4.6, and SD Post Mean=2.5).

Five patients excluded from the study and totally the number of patients for the final analysis was 35. To ensure that the study power is optimal, with the present study result parameters, the study power was calculated using Stata software (version 12.0, StataCorp, College Station, TX), which it obtained 93%.

The study was approved by the Local Ethical Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1395.1241). Verbal and written consent was obtained from all LOD subjects.

The serum levels of AMH and FSH were determined in all patients. Demographic parameters, such as age, body mass index (BMI), and duration of infertility, were recorded. The patients then underwent surgery based on the surgeon's estimation of the size of the ovaries regarding LOD, either unilateral or bilateral, with monopolar electrocautery and four punchers with the power of 30 W for 4 s. The serum levels of AMH and FSH were measured 3 months after surgery using available commercial enzyme immunoassay kits (CoBase and Elecsys, Roche Company).

The data were analyzed using Stata software. The process of data cleaning and exploration was done. The mean, SDs, and other dispersion indicators were utilized to describe quantitative variables, while the frequency tables and graphs were utilized to describe qualitative variables.

The Mann–Whitney non-parametric test was used to test the hypotheses of the study based on variables. A significant level of 0.05 was considered for all analyzes.

Results

A total of 35 female patients were enrolled in this study; 18 subjects had bilateral (51.4%) LOD, and 17 subjects (48.6%) had unilateral LOD. The average age was 27 ±3.4 years old. Descriptive characteristics of patients are presented in Tables 1 and 2.

Table 1. Descriptive Characteristics of PCOS Patients treated with LOD

		Number	Percent	Mean	S.D.
Age	Unilateral LOD	17	48.6%	26.64	3.60
	Bilateral LOD	18	51.4%	27.88	3.30
	Total	35	100.0%	27.28	3.46
BMI	Unilateral LOD	17	48.6%	26.47	3.20
	Bilateral LOD	18	51.4%	27.44	4.11
	Total	35	100.0%	26.97	3.68
Infertility Age	Unilateral LOD	17	51.4%	3.5	2.2
	Bilateral LOD	18	48.6%	3.83	1.9
	Total	35	100.0%	3.67	3.67

Table 2. FSH and AMH levels of PCOS Patients before and after treatment with LOD

		FSH before	FSH after	AMH before	AMH after
Unilateral LOD	Number	17	17	17	17
	Percent	48.6%	48.6%	48.6%	48.6%
	Mean	6.26	8.75	4.28	2.92
	S.D.	1.86	1.93	1.18	0.98
Bilateral LOD	Number	18	18	18	18
	Percent	51.4%	51.4%	51.4%	51.4%
	Mean	5.78	6.63	8.38	6.1
	S.D.	1.85	2.45	4.31	2.69

Based on the Mann–Whitney test, AMH serum levels in all patients after LOD had a statistically significant decrease (P<0.001).

AMH serum levels significantly decreased after LOD in unilateral (P<0.001) and bilateral (P=0.001) groups. There was no significant difference between two groups of unilateral and bilateral LOD in reducing AMH (P=0.507). FSH serum levels significantly increased in all patients after LOD (P<0.001). FSH levels increased significantly in unilateral LOD (P<0.001) and bilateral LOD (P<0.001). The increase of FSH in the unilateral group was higher than in the bilateral group, and the difference was statistically significant (P<0.001).

Discussion

Women with clomiphene-resistant PCOS when underwent unilateral or bilateral ovarian drilling experienced a decrease in their ovarian reserve; thus, more studies must be needed to consider it as a treatment choice for clomiphene citrate-resistant PCOS. However, no significant damage has yet been observed to the ovarian reserve after LOD **(21, 22)**.

In the study of Sunj *et al.*, the amounts of AMH and LH decreased significantly in the 1st and 6th months after LOD **(23)**. Also, in the study of Rezk *et al.*, AMH and LH significantly decreased in patients 3 months after LOD **(24)**, which were similar to the results of this study. However, in the study of Farzadi *et al.*, following laparoscopic ovarian surgery, serum levels of LH, AMH, and testosterone were not different in women with PCOS in 1 week and 3 and 6 months after surgery **(25)**.

Previous studies have shown that AMH is a better predictor of ovarian reserve than FSH in LOD, and the receiver operating characteristic (ROC) curve has also shown higher sensitivity and specificity of AMH **(26)**.

Studies have also shown that AMH levels in women with PCOS are significantly higher than in healthy women. As the severity of the disease increases, the serum level of AMH increases coordinately **(27)**. Plasma AMH concentration is a useful predictor of LOD outcomes. A serum level of 7.7 ng/mL of AMH before LOD significantly reduces the likelihood of ovulation after LOD **(28)**.

On the other hand, severe AMH reduction after LOD indicates excessive destruction of the ovarian antral and pre-enteral follicle, which secretes AMH and reduces the ovarian follicular reserve. In the physiological state, AMH decreased to less than 1 to 1.5 occurs at the end of the female reproductive age, and the serum AMH level predicts the reduction of ovarian follicular reserve. According to studies, reducing AMH less than 1 ng/mL can predict poor ovarian reserve, poor ovarian response to stimulation, and in vitro fertilization (IVF) outcomes **(29)**.

For future studies, the duration of the study will be longer, and the long-term effect of drilling on AMH and FSH levels will be investigated. In addition, due to the increase in androgens in PCOS and its importance in the return of fertility, except FSH and AMH, testosterone levels should also be evaluated.

Conclusion

It seems women with clomiphene-resistant PCOS when underwent unilateral or bilateral ovarian drilling experienced a significant decrease in AMH and a significant increase in FSH, indicating a decrease in their ovarian reserve.

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Conflict of Interest

Authors declared no conflict of interests.

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